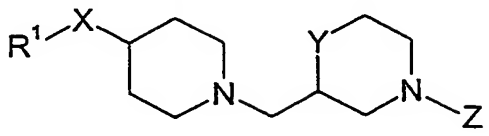
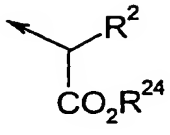
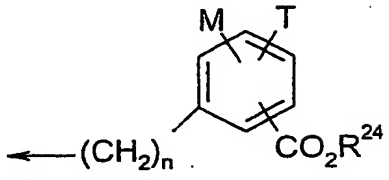
CLAIMS

1. A compound of formula (I):



(I)

wherein:

Z is  or 

n is 0 or 1;

X is CH_2, C(O), O, S, S(O), $S(O)_2$ or NR^3;

Y is O or CH_2;

R^1 is hydrogen, C_{1-6} alkyl, aryl or heterocyclyl;

R^2 is C_{3-7} cycloalkyl {optionally substituted by C_{1-4} alkyl, aryl or oxo}, C_{3-7} cycloalkenyl {optionally substituted by oxo, C_{1-6} alkyl or aryl}, aryl or heterocyclyl;

wherein the foregoing aryl and heterocyclyl moieties are optionally substituted by: halogen, cyano, nitro, hydroxy, oxo, $S(O)_pR^4$, $OC(O)NR^5R^6$, NR^7R^8, $NR^9C(O)R^{10}$, $NR^{11}C(O)NR^{12}R^{13}$, $S(O)_2NR^{14}R^{15}$, $NR^{16}S(O)_2R^{17}$, $C(O)NR^{18}R^{19}$, $C(O)R^{20}$, CO_2R^{21}, $NR^{22}CO_2R^{23}$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy(C_{1-6})alkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{1-6} alkoxy(C_{1-6})alkoxy, C_{1-6} alkylthio, C_{1-6} haloalkylthio, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl (itself optionally substituted by C_{1-4} alkyl or oxo), methylenedioxy, difluoromethylenedioxy, phenyl, phenyl(C_{1-4})alkyl, phenoxy, phenylthio, phenyl(C_{1-4})alkoxy, heterocyclyl, heterocyclyl(C_{1-4})alkyl, heterocyclyloxy or heterocyclyl(C_{1-4})alkoxy; wherein any of the immediately foregoing phenyl and heterocyclyl moieties are optionally substituted with halogen, hydroxy, nitro, $S(O)_q$(C_{1-4} alkyl), $S(O)_2NH_2$, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, $C(O)NH_2$, C(O)NH(C_{1-4} alkyl), C(O)N(C_{1-4} alkyl)$_2$ (and these alkyl groups may join to form a ring as described for R^5 and R^6 below), CO_2H, CO_2(C_{1-4} alkyl), NHC(O)(C_{1-4} alkyl), $NHS(O)_2$(C_{1-4} alkyl), C(O)(C_{1-4} alkyl), CF_3 or OCF_3;

M and T are, independently, hydrogen, halogen, cyano, nitro, hydroxy, oxo, $S(O)_pR^4$, $OC(O)NR^5R^6$, NR^7R^8, $NR^9C(O)R^{10}$, $NR^{11}C(O)NR^{12}R^{13}$, $S(O)_2NR^{14}R^{15}$, $NR^{16}S(O)_2R^{17}$, $C(O)NR^{18}R^{19}$, $C(O)R^{20}$, CO_2R^{21}, $NR^{22}CO_2R^{23}$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy(C_{1-6})alkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{1-6} alkoxy(C_{1-6})alkoxy, C_{1-6} alkylthio, C_{1-6} haloalkylthio, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl (itself optionally substituted by C_{1-4} alkyl or oxo), methylenedioxy, difluoromethylenedioxy, phenyl, phenyl(C_{1-4})alkyl, phenoxy, phenylthio, phenyl(C_{1-4})alkoxy, heterocyclyl, heterocyclyl(C_{1-4})alkyl, heterocyclyloxy or heterocyclyl(C_{1-4})alkoxy; wherein any of the immediately foregoing phenyl and heterocyclyl moieties are optionally substituted with halogen, hydroxy, nitro, $S(O)_q$(C_{1-4} alkyl), $S(O)_2NH_2$, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, $C(O)NH_2$, $C(O)NH(C_{1-4}$ alkyl), $C(O)N(C_{1-4}$ alkyl)$_2$ (and these alkyl groups may join to form a ring as described for R^5 and R^6 below), CO_2H, $CO_2(C_{1-4}$ alkyl), $NHC(O)(C_{1-4}$ alkyl), $NHS(O)_2(C_{1-4}$ alkyl), $C(O)(C_{1-4}$ alkyl), CF_3 or OCF_3;

p and q are, independently, 0, 1 or 2;

R^3, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{18}, R^{19}, R^{20}, R^{21} and R^{22} are, independently, hydrogen, C_{1-6} alkyl (optionally substituted by halogen, hydroxy or C_{3-10} cycloalkyl), $CH_2(C_{2-6}$ alkenyl), phenyl (itself optionally substituted by halogen, hydroxy, nitro, NH_2, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl)$_2$ (and these alkyl groups may join to form a ring as described for R^5 and R^6 below), $S(O)_2(C_{1-4}$ alkyl), $S(O)_2NH_2$, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, $C(O)NH_2$, $C(O)NH(C_{1-4}$ alkyl), $C(O)N(C_{1-4}$ alkyl)$_2$ (and these alkyl groups may join to form a ring as described for R^5 and R^6 below), CO_2H, $CO_2(C_{1-4}$ alkyl), $NHC(O)(C_{1-4}$ alkyl), $NHS(O)_2(C_{1-4}$ alkyl), $C(O)(C_{1-4}$ alkyl), CF_3 or OCF_3) or heterocyclyl (itself optionally substituted by halogen, hydroxy, nitro, NH_2, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl)$_2$ (and these alkyl groups may join to form a ring as described for R^5 and R^6 below), $S(O)_2(C_{1-4}$ alkyl), $S(O)_2NH_2$, $S(O)_2NH(C_{1-4}$ alkyl), $S(O)_2N(C_{1-4}$ alkyl)$_2$ (and these alkyl groups may join to form a ring as described for R^5 and R^6 below), cyano, C_{1-4} alkyl, C_{1-4} alkoxy, $C(O)NH_2$, $C(O)NH(C_{1-4}$ alkyl), $C(O)N(C_{1-4}$ alkyl)$_2$ (and these alkyl groups may join to form a ring as described for R^5 and R^6 below), CO_2H, $CO_2(C_{1-4}$ alkyl), $NHC(O)(C_{1-4}$ alkyl), $NHS(O)_2(C_{1-4}$ alkyl), $C(O)(C_{1-4}$ alkyl), CF_3 or OCF_3); alternatively NR^5R^6, NR^7R^8, $NR^{12}R^{13}$, $NR^{14}R^{15}$, $NR^{18}R^{19}$, may, independently, form a 4-7 membered heterocyclic ring, azetidine, pyrrolidine, piperidine, azepine,

1,4-morpholine or 1,4-piperazine, the latter optionally substituted by C_{1-4} alkyl on the distal nitrogen;

R^4, R^{17} and R^{23} are, independently, C_{1-6} alkyl (optionally substituted by halogen, hydroxy or C_{3-10} cycloalkyl), $CH_2(C_{2-6}$ alkenyl), phenyl (itself optionally substituted by halogen, hydroxy, nitro, NH_2, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl)$_2$ (and these alkyl groups may join to form a ring as described for R^5 and R^6 above), $S(O)_2(C_{1-4}$ alkyl), $S(O)_2NH_2$, $S(O)_2NH(C_{1-4}$ alkyl), $S(O)_2N(C_{1-4}$ alkyl)$_2$ (and these alkyl groups may join to form a ring as described for R^5 and R^6 above), cyano, C_{1-4} alkyl, C_{1-4} alkoxy, $C(O)NH_2$, $C(O)NH(C_{1-4}$ alkyl), $C(O)N(C_{1-4}$ alkyl)$_2$ (and these alkyl groups may join to form a ring as described for R^5 and R^6 above), CO_2H, $CO_2(C_{1-4}$ alkyl), $NHC(O)(C_{1-4}$ alkyl), $NHS(O)_2(C_{1-4}$ alkyl), $C(O)(C_{1-4}$ alkyl), CF_3 or OCF_3) or heterocyclyl (itself optionally substituted by halogen, hydroxy, nitro, NH_2, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl)$_2$ (and these alkyl groups may join to form a ring as described for R^5 and R^6 above), $S(O)_2(C_{1-4}$ alkyl), $S(O)_2NH_2$, $S(O)_2NH(C_{1-4}$ alkyl), $S(O)_2N(C_{1-4}$ alkyl)$_2$ (and these alkyl groups may join to form a ring as described for R^5 and R^6 above), cyano, C_{1-4} alkyl, C_{1-4} alkoxy, $C(O)NH_2$, $C(O)NH(C_{1-4}$ alkyl), $C(O)N(C_{1-4}$ alkyl)$_2$ (and these alkyl groups may join to form a ring as described for R^5 and R^6 above), CO_2H, $CO_2(C_{1-4}$ alkyl), $NHC(O)(C_{1-4}$ alkyl), $NHS(O)_2(C_{1-4}$ alkyl), $C(O)(C_{1-4}$ alkyl), CF_3 or OCF_3);

R^{24} is hydrogen, C_{1-6} alkyl or benzyl;

or an N-oxide thereof; or a pharmaceutically acceptable salt thereof; or a solvate thereof.

2. A compound of formula (I) as claimed in claim 1 wherein X is O.

3. A compound of formula (I) as claimed in claim 1 or 2 wherein Y is O.

4. A compound of formula (I) as claimed in claim 1 or 2 wherein Y is CH_2.

5. A compound of formula (I) as claimed in claim 1, 2, 3 or 4 wherein R^{24} is hydrogen.

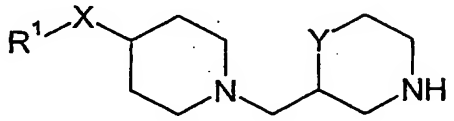
6. A compound of formula (I) as claimed in claim 1, 2, 3, 4 or 5 wherein R^1 is phenyl optionally substituted with fluorine, chlorine or C_{1-4} alkyl.

7. A compound of formula (I) as claimed in claim 1, 2, 3, 4, 5 or 6 wherein R^2 is phenyl or heterocyclyl, either of which is optionally substituted by: halo, hydroxy, nitro, cyano, amino, C_{1-4} alkyl (itself optionally substituted by $S(O)_2(C_{1-4}$ alkyl) or $S(O)_2$phenyl), C_{1-4} alkoxy, $S(O)_pR^4$ (wherein p is 0, 1 or 2), $C(O)NH_2$, $NHS(O)_2(C_{1-4}$ alkyl), $S(O)_2NH_2$, $S(O)_2NH(C_{1-4}$ alkyl) or $S(O)_2N(C_{1-4}$ alkyl)$_2$; and R^4 is C_{1-4} alkyl, C_{1-4} hydroxyalkyl, C_{3-7} cycloalkyl or C_{3-7} cycloalkyl(C_{1-4} alkyl).

8. A process for preparing a compound of formula (I) as claimed in claim 1, the process comprising:

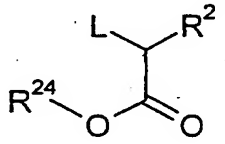
A. when Z is $CHR^2CO_2R^{24}$:

i. coupling a compound of formula (II):



(II)

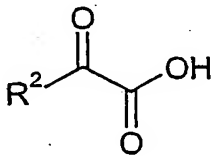
with a compound of formula (III):



(III)

wherein L is a suitable leaving group, in a suitable solvent; or,

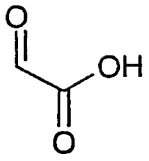
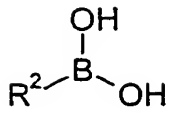
ii. reductive amination of a compound (II) with an ester compound of formula (IIIa):



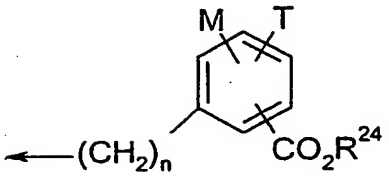
(IIIa)

in the presence of $NaBH(OAc)_3$ and acetic acid, followed optionally by removal of the ester group; or

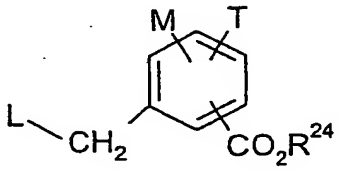
iii. a three component coupling of a compound of formula (II) with compounds of formula (IIIb) and (IIIc):


(IIIb)

(IIIc)

B. when

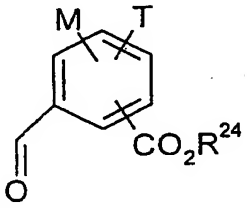
Z is 

a. when n is 1, reacting a compound of formula (II) with a compound of formula (XIV):


(XIV)

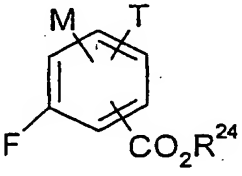
wherein L is a leaving group;

b. when n is 1, reacting a compound of formula (II) with a compound of formula (XVI):


(XVI)

under reductive amination conditions; and,

c. when n is 0, reacting a compound of formula (II) with a compound of formula (XV):


(XV)

in the presence of potassium carbonate, in a suitable solvent at a suitable temperature.

9. A pharmaceutical composition which comprises a compound of the formula (I), or a pharmaceutically acceptable salt thereof or solvate thereof as claimed in claim 1, and a pharmaceutically acceptable adjuvant, diluent or carrier.

10. A compound of the formula (I), or a pharmaceutically acceptable salt thereof or solvate thereof as claimed in claim 1, for use in therapy.

11. A compound of formula (I), or a pharmaceutically acceptable salt thereof or solvate thereof as claimed in claim 1, in the manufacture of a medicament for use in therapy.

12. A method of treating a chemokine mediated disease state in a mammal suffering from, or at risk of, said disease, which comprises administering to a mammal in need of such treatment a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof or solvate thereof as claimed in claim 1.